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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,223	06/29/2005	Heinz Schneider	09600-00031-US	9409

23416 7590 12/14/2007
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EXAMINER	
MCCORMICK, MELENIE LEE	
ART UNIT	PAPER NUMBER
1655	

MAIL DATE	DELIVERY MODE
12/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,223	SCHNEIDER, HEINZ	
	Examiner	Art Unit	
	Melenie McCormick	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-10,16,18,19 and 21-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-10,16,18,19 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants remarks with claim amendments submitted 26 September 2007 have been received and considered.

Claim 20 has been cancelled.

Claims 3-10, 16, and 18-19 and 21-25 are presented for examination on the merits.

The cancellation of claim 20 has overcome the previous rejection under 35 U.S.C. 112, second paragraph and the rejection under 35 U.S.C. 103 (a) as being unpatentable over Inanami et al. (Free Radic Res), Schnieider et al. (US 6,656,608) and Jerkic et al. (Nephr Dial Trans), and further in view of Wu et al. (J. Nutr.).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-10, 16, 18-19, 21 and 23-25 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition and a method for reducing the risk of postoperative ischemia reperfusion injury, does not reasonably provide enablement for a composition and a method which is effective in reducing the risk of any and all postoperative complications, as instantly claimed. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and/or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine and a method for reducing the risk of postoperative complication comprising the step of administering a composition which comprises green tea extract and at least one NO donor which is a substrate of NO synthetase, and/ or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine .

While Applicant has reasonably demonstrated the instantly claimed composition and method may be enabling for reducing the risk of postoperative ischemia reperfusion (see e.g. Specification- pgs 11-12), Applicant has not demonstrated that the instantly claimed composition and method are able to reduce the risk of all possible post-operative complications, which are encompassed by the instant claims.

As evidenced by Kerr et al., one possible postoperative complication is hypercapnia (see e.g. page 588, last para). Such a postoperative complication is encompassed by the instant claims, which read on any and all postoperative complications.

Nowhere in the specification as originally filed does Applicant demonstrate that the claim-designated composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and/or one precursor of this NO donor,

wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine and method for reducing the risk of postoperative complication comprising the step of administering a composition which comprises green tea extract and at least one NO donor which is a substrate of NO synthetase, and/ or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine is effective in reducing the risk of hypercapnia.

Thus, while Applicant has reasonably demonstrated a composition and method enabling reducing the risk of postoperative ischemia reperfusion following selected surgical procedures, Applicant has not demonstrated the claim-designated composition and method are effective in reducing the risk of all postoperative complications (including, for example, hypercapnia). Therefore, it would require undue experimentation without a reasonable expectation of success in order to determine the efficacy of the claim-designated composition and method in reducing the risk of any and all postoperative complications, as broadly claimed by Applicant.

Response to Arguments

Applicants argue that the usefulness of the formulations for averting or reducing the risk of postoperative complications is exemplified in the specification for ischemia reperfusion injury. This is not disputed. The instant enablement rejection states that while Applicant has reasonably demonstrated a composition and method enabling reducing the risk of postoperative ischemia reperfusion following selected surgical

procedures, Applicant has not demonstrated the claim-designated composition and method are effective in reducing the risk of all postoperative complications. Applicants also argue that the term "postoperative complications" encompasses different indications and is well-known in the art. Applicants have also provided a reference which lists a number of post operative complications. Applicants further argue that persons skilled in the art know and understand that even though various conditions may be present, these are still classified as postoperative conditions. This is not persuasive, however, because although a person skilled in the art would know that some types of reactions could be classified as post-operative complications, a person of ordinary skill in the art would not be able to determine, with a high amount of experimentation, which particular post-operative complications could be reduced by the instantly claimed method. Based on the wide range of post-operative complications which may occur, it would take undue experimentation without a reasonable expectation of success for a person of ordinary skill in the art to determine which particular post operative complications could be reduced by the instantly claimed method. For example, Clavien et al. (provided by Applicants), discloses that particular infections (see e.g. page 521) are postoperative complications. Applicants have not demonstrated that the instantly claimed method would be effective in reducing the risk of infection. Therefore, Applicants are not enabled for the full scope of the instant claims.

The rejection is therefore deemed proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-10, 16, 18-19, and 21-25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Inanami et al. (Free Radic Res), Schnieider et al. (US 6,656,608), Sherrat et al. (US 6,423,349), and Schnieder et al. (5,902,829).

A formulation for gastrointestinal administration to a surgical patient before a surgical procedure to reduce the risk of postoperative complications or to avert such a risk comprising a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine is claimed. A method of averting or reducing the risk of postoperative complications comprising the step of gastrointestinally administering to a surgical patient a composition comprising green tea extract and at least one NO donor which is a substrate of NO synthetase, and or one precursor of this NO donor, wherein the NO donor and precursor are selected from a group which consists of glutamine and nitroglycerine is also claimed.

Inanami et al. beneficially teach the protective effects of the green tea polyphenol (-) catechin against damage in the brain caused by ischemia in gerbils. Inanami et al.

further teach that the compound is intended to be orally (gastrointestinally) administered prior to a reperfusion event (surgery)- see entire document including abstract and methods. Please note that theanine is one of the predominant amino acids present in green tea, and would intrinsically be present in an extract of green tea. Inanami et al. do not expressly teach that the composition further comprises glycine or at least one NO donor which is a substrate of NO synthetase.

Schneider et al. '608 beneficially teach that glycine is useful in protecting against damage caused by ischemia reperfusion. Schneider et al. further beneficially teach that a composition comprising glycine is intended to be administered orally (see e.g. col 5 line 66-col 6 line 2). Schneider et al. also further beneficially teach that the composition is intended as a pre-operative treatment (see e.g. col. 6 lines 21-23).

Sherratt et al. beneficially teach a composition and a method of administering a composition to patients prior to elective surgery in order to protect against ishchemia reperfusion (see e.g. col 4, lines 35-45 and col 5, lines 1-3 and 42-45). Sherratt et al. further teach that nitroglycerin is useful in this method and composition to decrease reperfusion injury (see e.g. col 4, lines 53-66). It is further disclosed by Sherratt et al. that reperfusion injury is attenuated by administration of free radical scavengers (see e.g. col 5, lines 5-7). Sherratt et al. further teach that glutamine is a free radical scavenger and that glutamine is administered to patients in order to promote the recovery of elective surgery (see e.g. col 5, lines 22-37 and lines 45-63 and claim 1). Sherrat et al. further teach that the composition is administered to patients prior to

elective surgery, particularly for two days prior to the surgery (see e.g. claim 9) and that the administration is oral or via a feeding tube (see e.g. col 10, lines 8-10).

Schneider et al. '829 beneficially teach a composition and a method of administering the composition pre-operatively which reduces the risk of reperfusion injury in patients who undergo elective surgery (see e.g. col 1, lines 21-26). Schneider et al. further teach that L-arginine or a precursor of L-arginine is used for this purpose (see e.g. col 1, lines 27-34). It is further disclosed by Schneider et al. a precursor of L-arginine which may be used pre-operatively is glutamine (see e.g. col 1, lines 35-36 and claim 4).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the green tea extract taught by Inanami et al. and the glycine and glutamine taught by Schneider et al. '608 and Sherratt et al. and Schneider '829, respectively, to obtain a composition which would be useful for treating preoperative patients to reduce the risk of post operative complications (such as the oxidative injury caused by ischemia reperfusion). Since it is well known in the art that the majority of damage resulting from ischemia reperfusion is related to oxidative stress, it would have been obvious to the skilled artisan and the skilled artisan would have been motivated and would have had a reasonable expectation of success in combining a well known antioxidant (green tea extract) with glutamine, especially since, as disclosed by Sherratt and Schneider et al. '829, glutamine is useful in protecting against of post operative reperfusion injury. Since it has also been shown that glycine may be useful as a treatment to protect against ischemia reperfusion (as disclosed by Schneider et al.

'608), it would have been obvious to include this compound in composition which was to be used for the same purpose. Please note that the administration times taught by the instantly cited references would render obvious the instantly claimed administration which takes place less than twenty four hours prior to surgery because the references teach administration which *begins* before the surgery. Administration that begins any time prior to surgery and continues until the surgery would be taking place less than twenty four hours prior to surgery, as instantly claimed. The adjustment of particular conventional working conditions (e.g. administering the composition to a patient at a hour before or after surgery) is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan.

Response to Arguments

Applicants argue that the instantly claimed compositions and methods are not obvious in view of Inanami et al., Schneider et al. '608, Sherrat et al. or Schneider et al. '829. Applicants further argue that none of the references, alone or in any combination disclose or suggest the claimed invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In response to Applicants arguments that the combination of the references would not disclose or suggest the instantly claimed invention, as previously stated, a person of ordinary skill in the art would have had a reasonable expectation of success in combining the instantly claimed

components since each was used in the art for the same purpose. Specifically, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the green tea extract taught by Inanami et al. and the glycine and glutamine taught by Schneider et al. '608 and Sherratt et al. and Schneider '829, respectively, to obtain a composition which would be useful for treating preoperative patients to reduce the risk of post operative complications (such as the oxidative injury caused by ischemia reperfusion). Since it is well known in the art that the majority of damage resulting from ischemia reperfusion is related to oxidative stress, it would have been obvious to the skilled artisan and the skilled artisan would have been motivated and would have had a reasonable expectation of success in combining a well known antioxidant (green tea extract) with glutamine, especially since, as disclosed by Sherratt and Schneider et al. '829, glutamine is useful in protecting against of post operative reperfusion injury. Since it has also been shown that glycine may be useful as a treatment to protect against ischemia reperfusion (as disclosed by Schneider et al. '608), it would have been obvious to include this compound in composition which was to be used for the same purpose.

Applicants also argue that Applicants have found unexpected results and have provided a declaration. Applicant's invention is predicated on an unexpected result, which typically involves synergism, an unpredictable phenomenon, highly dependent upon specific proportions and/or amounts of particular ingredients. Any mixture of the components embraced by the claims which does not exhibit an unexpected result (e.g. synergism) is therefore *ipsto facto* unpatentable. Applicant's claims are not

commensurate in scope with the particular conditions which would lead to an unexpected result as disclosed in the declaration.

The rejection is therefore deemed proper and is maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melenie McCormick whose telephone number is (571) 272-8037. The examiner can normally be reached on M-F 7:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Melenie McCormick
Examiner
Art Unit 1655